REMARKS

The Applicants thank the Examiner for the courteous telephone interview initiated by the Examiner on March 13, 2003. Present on the phone during the interview were Examiner Audet, Applicant's counsel Stephen Holmes, and co-applicant Dale DeVore.

During the interview, the Examiner requested clarification of certain protein (collagen) derivatizations. As explained by co-applicant Dale Devore, the specific derivatives were formed to make collagen more negatively charged and to attach pendant sulfhydryl groups. The former appears to help adhesiveness and the latter appears to improve cohesiveness.

Applicant further thanks the Examiner for the short telephone interview on August 18, 2003 during which proposed amendments to the claims, and proposed responses to the Section 112 rejections were discussed. No agreement was reached. The Examiner will review further upon submission of the formal amendment.

In the Office Action, the Examiner indicated that claims 17-25 are withdrawn from consideration; rejected claims 1-16 under 35 U.S.C. § 112, first paragraph; rejected claims 1-16 under 35 U.S.C. § 112, second paragraph; rejected claims 1, 4-9, and 14-16 under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,495,127 to Wallace et al.; rejected claims 1-10 and 14-16 under 35 U.S.C. § 102(b) as being anticipated 5,219,895 to Kelman et

al.;[1] rejected claims 1-16 under 35 U.S.C. § 103(a) as being unpatentable over Wallace et al. in view of Kelman et al. and U.S. Patent No. 6,161,544 to DeVore et al.; and rejected claims 1-16 under 35 U.S.C. § 103(a) as being unpatentable over Wallace et al. in view of an article to Caroli et al. and further in view of U.S. Patent No. 5,767,152 to Nielson et al.

Applicants have amended claims 1-3, 5 and 10; canceled claims 11-13, 15 and 17-25; and added new claims 26-42. Claims 1-10, 14, 16 and 26-42 are pending in the present application.

At the outset, Applicants respectfully point out that previously withdrawn claims 17-25 have now been cancelled by this Amendment.

Applicants have amended claim 1, for example, to recite a composition having a concentration of collagen and is not limited by language directed to derivatized collagen in particular. New claim 1 also recites that the concentration of collagen is at least equal to 300 mg/ml but not more than 800 mg/ml. Applicants note that the specification provides support for both derivatized and non-derivatized formulations, see for example, page 11, lines 15-16 ("Additional solder formulations were prepared from collagen derivatized with glutaric anhydrided only or from non-derivatized acid soluble collagen." Note also page 10, line 2.) Accordingly, Applicants submit that claim 1 without limitations requiring

[1] Applicants respectfully note that the first two lines of page 14 of the Office Action indicate that claims 1-10 and 14-16 are rejected under 35 U.S.C. § *102(e)* as being anticipated by *Wallace et al.* even though a Section 102 rejection based on Wallace et al. is previously articulated on page 13, and the text of the Office Action following the first two lines of page 14 refers to the Kelman et al. reference. Accordingly, Applicants assume the Examiner intended to reject claims 1-10 and 14-16 under 35 U.S.C. § 102(b) as being anticipated by Kelman et al.

derivatized collagen is adequately supported by the specification.

New independent claim 36, which is similarly not limited to derivatized collagen is also believed to be adequately supported by Applicants' disclosure.

Turning to the rejections, Applicants respectfully traverse the Examiner's rejection of claims 1-16 under 35 U.S.C. § 112, first paragraph. Applicants respectfully submit that the Examiner's rejection with respect to claim 1 is moot in view of Applicants' amendment to claim 1 in which language related to derivatization has been redacted.

At pages 2-5 of the Office, the Examiner contends that the specification only supports claim language directed toward collagen derivatized with both carboxyl (COO^-) and thiol (SH^-) functional groups. In particular, the Examiner quotes page 9 of Applicants' specification describing enhancement of solder adhesive and cohesive characteristics by adding both carboxyl and thiol groups (see Office Action at page 4). The Examiner then concludes that the specification describes "throughout" such groups are "needed" for cohesive and adhesive strength, and suggest that in order to overcome the rejection, Applicants amend independent claim 1 to recite collagen derivatized with both carboxyl and thiol groups. Applicants respectfully disagree with the Examiner's characterization of their disclosure, and submit that such language in their broadest claims would unduly limit the scope of their invention.

Applicants respectfully submit, however, that the specification is not only directed toward formulations having collagen derivatized with both carboxyl and thiol groups. Rather, derivatization with carboxyl groups without thiol groups is expressly described in the specification at page 10, lines 6-8 ("Solder formulations were prepared from chemically derivatized Type 1 collagen. Base compositions contained either COO^- functional groups or both SH^- (thiol) and COO^- functional groups."; see also page 10, line 10: "Base preparations contained only COO^-)groups".) The specification even contemplates non-derivatized collagen formulations, which can provide superior results ("Additional solder formulations were prepared from collagen derivatized with glutaric anhydride only or from non-derivatized acid soluble collagen ... These collagen-based solder appeared to provide the best biomechanical and adhesive characteristics." Page 11, lines 15-20). The specification thus provides support for collagen compositions including collagen derivatized with carboxyl groups, carboxyl groups with thiol groups, and even no derivatization at all.

Moreover, Applicants respectfully submit that the portions of the specification discussed in the Office Action do not support the Examiner's conclusions. Those portions of the specification quoted in the Office Action describe a particular example of the invention in which collagen is derivatized with both carboxyl and thiol to enhance, i.e., improve, certain characteristics, namely

adhesive and cohesive strength, of the resulting adhesive. Such disclosure, however, does not mean that without carboxyl and thiol derivatization, the resulting adhesive is somehow inoperable or unsuitable for its intended purposed. To the contrary, even without such dual derivatization, suitable adhesives can be obtained. (See page 11, lines 15-20 noted above.)

Amended claim 2 and new claim 37, which recite collagen derivatized with a carboxyl group are thus supported by portions of the specification discussed above, as well as those cited in the Office Action. Further, independent claims 1, 26 and 36, which are not limited to derivatization, are also adequately supported by the specification.

Simply put, there is no language in the specification specifically limiting Applicants invention to collagen derivatized with both carboxyl and thiol groups. To the contrary, as noted above, the specification also provides support for carboxyl derivatization, and even no derivatization at all. Accordingly, incorporation of the suggested claim limitations (see page 4 of the Office Action) in Applicants' broadest claims, as suggested in the Office Action, would unduly limit the scope of the claims, and preclude Applicants from obtaining a scope of protection they are rightfully entitled to.

Although Applicants respectfully disagree with the Examiner's position that only collagen concentrations within a range of 300 mg/ml to 800 mg/ml are supported by the specification (see Office

Action at pages 5-7), Applicants have amended claim 1 to further recite that collagen concentration that is "not more than 800 mg/ml," in view of language proposed by the Examiner at page 7 of the Office Action.

Applicants also respectfully disagree with the arguments raised by the Examiner at pages 7-10 of the Office Action with respect to the cyanoacrylate-related limitation in claims 11-13. In order to advance prosecution of the present application, however, Applicants have cancelled claims 11-13, and submit that the Examiner's rejection is moot with respect to these claims.

Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the rejection under 35 U.S.C. § 112, first paragraph.

Applicants respectfully traverse the Examiner's rejection of claims 1-16 under 35 U.S.C. § 112, second paragraph. The Examiner alleges at page 10 of the Office Action that "[i]t is unclear whether Applicant is claiming a composition with derivatized collagen (an entire amount) or merely a concentration of derivatized collagen?" To the extent the Examiner's position is understood and in an effort to expedite prosecution of the present application, Applicants have amended claim 1 to recite a composition having a concentration of collagen, in units of milligrams per milliliter, which is at least equal to 300 mg/ml but not more than 800 mg/ml. Applicants respectfully submit that the changes to claim 1 resolve any alleged ambiguity in the

claims.

The Examiner further contends that claim 1 is indefinite because Applicants allegedly did not disclose in the specification "where the functional groups in question were to be attached within the collagen molecule." (See Office Action at page 11.) Applicants respectfully disagree.

The specification at page 10, lines 6-10 states:

> Base compositions contained either COO^- functional groups or both SH^- (thiol) and COO^- functional groups. The degree of derivatization with SH^- functional groups was varied in attempts to modulate cohesive characteristics. Remaining free amine groups on the native collagen molecule were derivatized with COO^- groups.

Emphasis added.

This cited portion of the specification expressly describes that derivatization occurs at the location of free amine groups on the native collagen molecule. Thus, the specification does indeed describe where carboxyl or thiol groups are attached during derivatization.

Further with respect to the Examiner's rejection under Section 112, second paragraph, Applicants have amended claim 5 to correct for antecedent basis. Moreover, Applicants respectfully submit that the Examiner's position in regard to carboxyl and thiol functional groups was addressed above with respect to the rejection under Section 112, first paragraph. Applicants further disagree that with the Examiner query as to whether the invention is a composition with both cohesive and adhesive strength or a composition with only cohesive or adhesive strength" (see Office

Action at page 11.) Applicants respectfully submit that the claims are not limited to particular values of cohesive or adhesive strengths. Rather, Applicants' invention is defined by the claims, which as amended, recite among other features, a composition having a range of collagen concentrations. Applicants further respectfully submit that the assertions contained in the Office Action to the contrary are both legally and factually misplaced.

Turning to claims 8 and 11-13, Applicants submit that the Examiner's position is moot in light of Applicants' cancellation of claims 11-13.

In view of the foregoing, Applicants respectfully request the Examiner to reconsider and withdraw the rejection under 35 U.S.C. § 112, second paragraph.

Applicants respectfully traverse the Examiner's rejection of claims 1, 4-9 and 14-16 under 35 U.S.C. § 102(e) as being anticipated by Wallace et al. Applicants respectfully submit that the rejection is moot with respect to claim 15 in light of the cancellation of this claim. However, amended claim 1, for example, is not anticipated by Wallace et al. because the reference fails to teach each and every limitation of the claim. In particular, Wallace et al. at least fails to disclose the claimed composition having a concentration of collagen such that the concentration of collagen is at least equal to 300 mg/ml but not more than 800 mg/ml.

The Examiner cites col. 27, line 10 of Wallace et al., and asserts that the reference teaches a "composition comprising derivatized collagen ... being at least equal to 300 mg or 400 mg to 800 mg". (See Office Action at page 13.) Applicants respectfully point out, however, that the cited portion of Wallace et al. describes mixing various materials with "400 mg of methylated collagen at 31 mg protein/ml." (Emphasis added.) Apparently, although Wallace et al. teaches adding 400 mg of collagen to a mixture, the concentration of that collagen is only 31 mg/ml, much less than the claimed range of concentrations of 300 mg/ml to 800 mg/ml. Wallace et al., therefore, necessarily fails to teach the claimed composition having the specified range of collagen concentrations, as recited in amended claim 1.

Accordingly, amended claim 1 is allowable over Wallace et al. and claims 4-9, 14 and 16 are allowable at least due to their dependence from amended claim 1.

Applicants respectfully traverse the Examiner's rejection of claims 1-10 and 14-16 under 35 U.S.C. § 102(b) as being anticipated by Kelman et al. The Examiner asserts that Kelman et al. teach a collagen composition "with at least one of an acylating agent ... and sulfonating agent ... to derivatize collagen ... which could intrinsically yield 300-800 mg if derivatized to said degree". Applicants respectfully submit that in order for a reference to anticipate under Section 102, each and every claim limitation must be found in the reference. Whether an omitted

teaching "could intrinsically" be present is not the test for anticipation. The Examiner has thus failed to establish anticipation based on Kelman et al. at least for this reason.

Moreover, even if Kelman et al. disclosed 300-800 mg of derivatized collagen, such teachings would be insufficient to anticipate claim 1, for example. As noted above, claim 1 recites a concentration of collagen in units of mg/ml, not just the weight of collagen present in a composition. Mere disclosure of the weight of collagen, by itself, does not indicate in any way the concentration of the collagen in terms of mass per unit volume, as required by amended claim 1.

Further, the cited portions of Kelman et al. are limited to disclosure of an amount of acylating agent to be mixed in a collagen solution (col. 5, line 1); performing acylation in an alkaline pH (col. 5, line 6); recovering a precipitate of reacted collagen containing substituent groups reacted with amine groups (col. 5, lines 28-30); and adjusting pH to 7.0 to 7.5 (col. 5, lines 38-40). None of the above teachings of Kelman et al. describe collagen concentration whatsoever, and thus necessarily fail to teach the claimed range of concentrations, as recited in amended claim 1.

Applicants respectfully traverse the Examiner's rejection of claims 1-16 under 35 U.S.C. § 103(a) as being unpatentable over Wallace et al. in view of Kelman et al. and DeVore et al.; and the rejection of claims 1-16 under 35 U.S.C. § 103(a) as being

unpatentable over Wallace et al. in view of an article to Caroli et al. and further in view of Nielson et al. The Examiner relies on teachings of DeVore et al. allegedly for disclosing "use of 4-Mercapto-1,8,Napthalic Anhydride" and teachings of Caroli et al. and Nielson et al. for allegedly for disclosing cyanoacrylate as a tissue adhesive with collagen (Caroli et al.) and that cyanoacrylate may be used externally (Nielson et al.) Applicants respectfully submit that the Examiner's rejection is moot with respect to cyanoacrylate-related claims 11-13. In any event, Applicants respectfully submit that even if such teachings were combinable in the manner proposed by the Examiner, the resulting combination of references would still fail to teach each and every limitation of claim 1, including the claimed range of collagen concentrations. Accordingly, DeVore et al., Caroli et al. and Nielson et al. fail to overcome the above-described deficiencies of Wallace et al. and Kelman et al., and claim 1 is allowable at least for reasons discussed above. Moreover, pending claims 2-10, 14 and 16 are allowable at least due to their dependence from amended claim 1.

Turning to new claims 26-42, new independent claims 26 and 36 recite a composition having a collagen concentration at least equal to 300 mg/ml but not more than 800 mg/ml. In addition, the collagen in the composition is derivatized with both carboxyl and thiol groups (claims 26, 37 and 38). Accordingly, in light of the above discussion in connection with the Examiner's rejections

under 35 U.S.C. § 112, first and second paragraphs, as well as the cited portion of the specification with respect to claim 36, Applicants submit that claim 26, 36, 37 and 38 meet the requirements of Section 112.

In addition, new claims 27-29 and 32, as well as new claims 39-42, parallel claims 4, 5, 6 and 9, respectively, and are thus deemed to satisfy the requirements of Section 112. Further, new claims 30, 31, and 33-35 track claims 7, 8, 10, 14 and 16, and are therefore also considered to meet the requirements of Section 112.

Moreover, since claims 26 and 36 are similar to claim 1 in reciting a collagen concentration at least equal to 300 mg/ml but not more than 800 mg/ml, Applicants submit that claims 26 and 36 are allowable over the applied references for reasons discussed above, and claims 27-35 and claims 37-42 are allowable at least due to their dependence from claims

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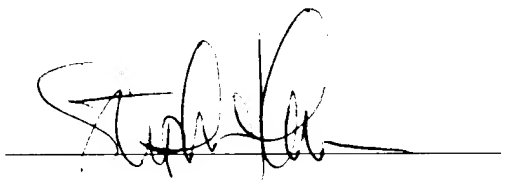
Respectfully submitted,

By: 

Stephen Holmes
Reg. No. 34,621

BARLOW, JOSEPHS & HOLMES, Ltd.
101 Dyer Street
5th Floor
Providence, RI 02903
401-273-4446 (tel)
401-273-4447 (fax)
sjh@barjos.com